



UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

100-43163-0

5 October 2010

MEMORANDUM

SUBJECT: Agreement on a common NCEL for the [REDACTED]
intermediates: P10-0326, [REDACTED]
[REDACTED]

FROM: Steven T. Cragg, PhD, DABT - Toxicologist *Steven T. Cragg 5-Oct-2010*
New Chemicals Screening and Assessment Branch
Risk Assessment Division

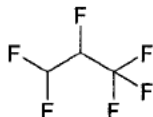
THRU: Robert E. Morcock, PhD - Branch Chief *Robert E. Morcock*
New Chemicals Screening and Assessment Branch
Risk Assessment Division (7403M) *5 OCT 10*

TO: Kristan Markey - Program Manager
New Chemicals Pre-Notice Branch
Chemical Control Division (7504M)

[REDACTED]

Within the last year, [REDACTED] Corporations have submitted a series of 3-carbon, variously fluorinated propanes [REDACTED] intended as [REDACTED] intermediates [REDACTED] for listing on the TSCA Inventory. Molecular structures and other identifying information are shown in the following table:

P10-0326 [REDACTED]



Propane, 1,1,1,2,3,3-hexafluoro-
CAS# 431-63-0
M.W. 152.04

8



5 0 1 1 0 0 0 0 2 3 6

In addition to the above cases, additional cases have been submitted

In a review of the toxicity literature for P10-0326 specifically (see Attachment 1), L. Russell and E. Margoshes developed NCELS for various toxicity endpoints for the fluorinated alkane (P10-0326) from NOAELs or benchmark doses estimates. The table containing NOAELs, and a BMDL along with corresponding NCELS is reproduced below. The NCELS were derived by dividing the NOAEL or BMDL by a factor of 10 to account for interspecies variability and another factor of 3 to protect the most sensitive individual in a healthy worker population.

Summary Table of NCELS for PMN10-326

PMN	ENDPOINT	NOAEL	BMDL	NCEL
P-10-326	Developmental	5000 ppm		166.7 ppm
	Reproductive	20000 ppm		666.7 ppm

The reproductive effects from exposure to the were found in rabbits, a species often more sensitive for developmental and reproductive effects than rats. Only rats were tested for developmental and reproductive effects for the fluorinated alkane (P10-0326). As a consequence the lowest NCEL for will be applied to all of the alkanes until such time as rabbit data are developed for the alkanes showing adverse effects only at higher concentrations.

The 1.7 ppm NCEL is rounded to 2 ppm, which will apply to all 3-carbon fluorinated alkane intermediates until further data may be developed.

cc: E. Margoshes
L. Russell
P. Sayre

Attachment 1

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RAD DISPOSITION MEETING

07 July 2010

I. BACKGROUND DATA:

Production Volume (P10-326)

Production Volume

Day 90: 30 July 2010

SUBMITTER ID:

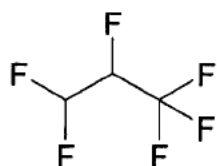
PROGRAM MANAGER: Kristan Markey

TOXICOLOGIST/ TECHNICAL INTEGRATOR:

Lemuel T. Russell, IV, Ph.D.

CHEMICAL ID: PMN substance P-10-0326, P10-0326, Propane, 1,1,1,2,3,3-hexafluoro- (CASRN 431-63-0).

USES: Chemical intermediate



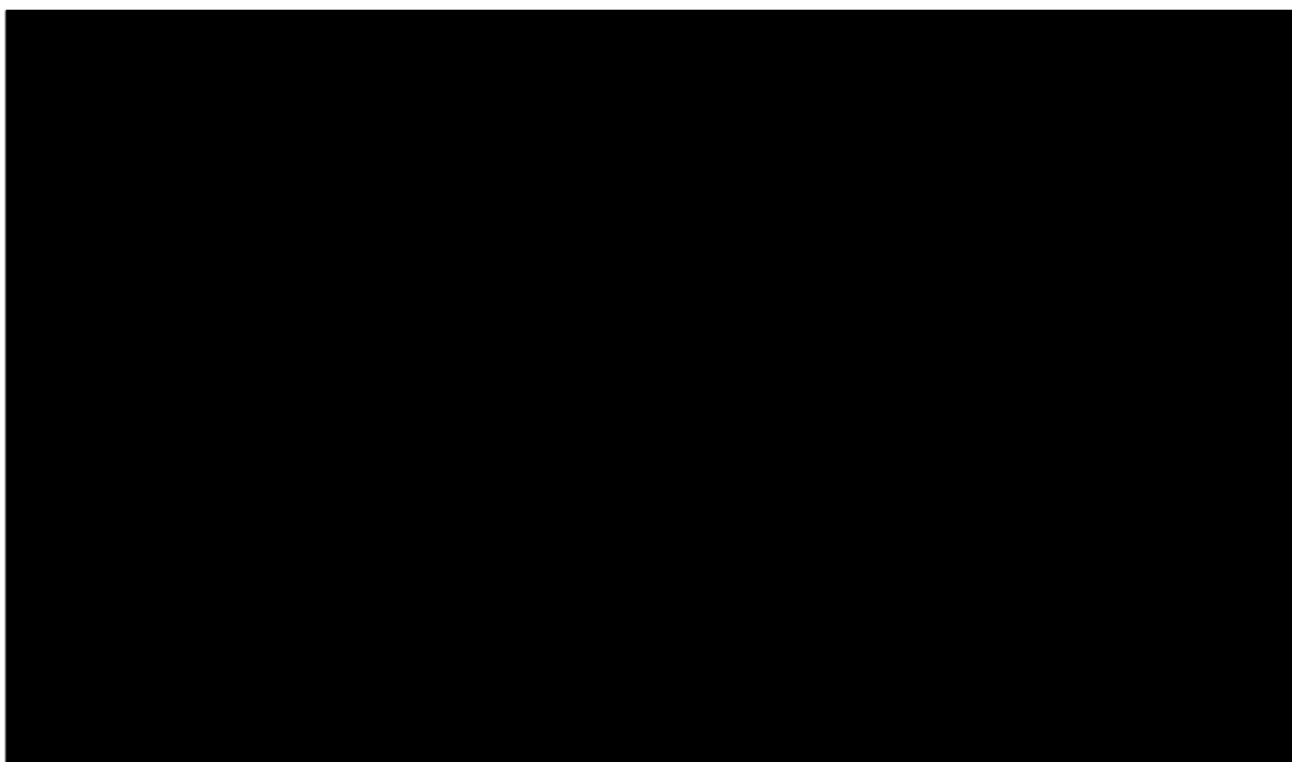
P10-326

Figure 1. Chemical structure of PMN substances P10-326

DATA SUBMITTED WITH CASE:

P10-326

Negative in a mutation assessment assay with *Salmonella* with and without activation; Negative in a mutation assessment assay with *E. coli* with and without activation; Negative for inhalation mouse micronucleus assay; Negative in a human lymphocyte assay with and without activation; rat 2-week inhalation NOEC = 5000 ppm, altered response to alerting stimulus at 20,000 and 50,000 ppm; dog cardiac sensitization NOEL = 2.5%, LOEL = 3.5%, 2/5 died at 10% [REDACTED]; rat inhalation LC50 = 85,000 ppm, narcosis at 24,000 ppm and higher ([REDACTED]; acute NOEC = 14,000 ppm); rat inhalation developmental NOEC = 50,000 ppm, maternal NOEC = 5000 ppm [REDACTED]; rat 14-week (90-day) inhalation NOEC = 5000 ppm, effects on testes at 50,000 ppm, change in response to alerting stimulus at 20,000 and 50,000 ppm ([REDACTED])



PMN	Type of Concern	Level of Concern	P	B	T
P10-326	Health	1-2	3	1	1

II. EXPOSURE LIMIT SUMMARY:

A. Health Hazard Report

Hazard concerns were expressed for:

- a. maternal, reproductive and developmental toxicity.
- b. systemic toxicity

Maternal, Reproductive and Developmental Toxicity

1. PMN P10-0326

Based on the observations of a developmental study conducted in rats and a 90-day repeated-dose study in rats, there appears to be limited cause for concern for maternal,

developmental or reproductive toxicity of PMN P-10-0326. In the developmental study, based on diminished alerting responses in dams, the NOAEL for maternal toxicity is 5000 ppm and the LOAEL is 10,000 ppm. Based on increased incidence of retarded sternebral ossification, the NOAEL for developmental toxicity appears to be 5000 ppm and the LOAEL is 20,000 ppm. In the 90-day study, increased testicular weights, increased testes-to-brain weight ratios, and dilatation of the seminiferous tubules when compared to controls was observed at 50,000 ppm. Thus, the reproductive toxicity NOAEL, based on testicular effects, was 20,000 ppm and the LOAEL was 50,000 ppm.

However, PMN P-10-0326 was only tested in rats, but not rabbits. The results observed suggest that rabbits may be more sensitive to the toxic effects of P-10-0326. Therefore, additional testing of rabbits in a two-generation reproductive toxicity study (OECD 416) is recommended.

B. New Chemical Exposure Limit (NCEL)

A New Chemical Exposure Limit (NCEL) may be derived from the BMDL or NOAEL for P10-326, based on effects observed on the endpoint of concern, by dividing the BMDL or the NOAEL by: 1) a factor of **10** to account for the uncertainty for extrapolating between species (rats to humans) ; 2) a factor of **03** to account for the uncertainty in protecting the most sensitive members of a healthy worker population.

$$\text{NCEL} = [\text{BMDL or NOAEL} / (10)(03)]$$

Summary Table of NCELs for PMN10-326

PMN	ENDPOINT	NOAEL	BMDL	NCEL
P-10-326	Developmental	5000 ppm		166.7 ppm
	Reproductive	20000 ppm		666.7 ppm

Health Hazard Citations

1. Neurotoxicity	Dr. Russell
2. Systemic Toxicity	Dr. Murphy
3. Carcinogenicity	Dr. Woo
4. Immunotoxicity	Dr. Ward
5. Developmental and Reproductive Toxicity	Dr. Cary
6. Statistical Support	Dr. Margosches